



## N-acetylglutamate synthase deficiency

N-acetylglutamate synthase deficiency is an inherited disorder that causes ammonia to accumulate in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

N-acetylglutamate synthase deficiency may become evident in the first few days of life. An infant with this condition may be lacking in energy (lethargic) or unwilling to eat, and have a poorly controlled breathing rate or body temperature. Some babies with this disorder may experience seizures or unusual body movements, or go into a coma. Complications of N-acetylglutamate synthase deficiency may include developmental delay and intellectual disability.

In some affected individuals, signs and symptoms of N-acetylglutamate synthase deficiency are less severe, and do not appear until later in life. Some people with this form of the disorder cannot tolerate high-protein foods such as meat. They may experience sudden episodes of ammonia toxicity, resulting in vomiting, lack of coordination, confusion or coma, in response to illness or other stress.

### Frequency

N-acetylglutamate synthase deficiency is a very rare disorder. Only a few cases have been reported worldwide, and the overall incidence is unknown.

### Genetic Changes

Mutations in the *NAGS* gene cause N-acetylglutamate synthase deficiency.

N-acetylglutamate synthase deficiency belongs to a class of genetic diseases called urea cycle disorders. The urea cycle is a sequence of reactions that occurs in liver cells. This cycle processes excess nitrogen, generated when protein is used by the body, to make a compound called urea that is excreted by the kidneys.

The *NAGS* gene provides instructions for making the enzyme N-acetylglutamate synthase, which helps produce a compound called N-acetylglutamate. This compound is needed to activate another enzyme, carbamoyl phosphate synthetase I, which controls the first step of the urea cycle.

In people with N-acetylglutamate synthase deficiency, N-acetylglutamate is not available in sufficient quantities, or is not present at all. As a result, urea cannot be produced normally, and excess nitrogen accumulates in the blood in the form of ammonia. This accumulation of ammonia causes the neurological problems and other signs and symptoms of N-acetylglutamate synthase deficiency.

## **Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## **Other Names for This Condition**

- hyperammonemia, type III
- N-acetylglutamate synthetase deficiency
- NAGS deficiency

## **Diagnosis & Management**

### Genetic Testing

- Genetic Testing Registry: Hyperammonemia, type III  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268543/>

### Other Diagnosis and Management Resources

- GeneReview: Urea Cycle Disorders Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1217>
- MedlinePlus Encyclopedia: Hereditary Urea Cycle Abnormality  
<https://medlineplus.gov/ency/article/000372.htm>
- National Organization for Rare Disorders (NORD) Physician Guide: Urea Cycle Disorders  
<http://nordphysicianguides.org/urea-cycle-disorders/>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

## **Additional Information & Resources**

### MedlinePlus

- Encyclopedia: Hereditary Urea Cycle Abnormality  
<https://medlineplus.gov/ency/article/000372.htm>
- Health Topic: Genetic Brain Disorders  
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Metabolic Disorders  
<https://medlineplus.gov/metabolicdisorders.html>

### Genetic and Rare Diseases Information Center

- N-acetylglutamate synthetase deficiency  
<https://rarediseases.info.nih.gov/diseases/7158/n-acetylglutamate-synthetase-deficiency>

### Educational Resources

- Disease InfoSearch: Hyperammonemia, type III  
<http://www.diseaseinfosearch.org/Hyperammonemia%2C+type+III/8576>
- Genetics Education Materials for School Success (GEMSS)  
<http://www.gemssforschools.org/conditions/urea-cycle/default>
- MalaCards: n-acetylglutamate synthase deficiency  
[http://www.malacards.org/card/n\\_acetylglutamate\\_synthase\\_deficiency](http://www.malacards.org/card/n_acetylglutamate_synthase_deficiency)
- Orphanet: Hyperammonemia due to N-acetylglutamate synthase deficiency  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=927](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=927)
- Screening, Technology and Research in Genetics  
<http://www.newbornscreening.info/>

### Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases  
<http://www.climb.org.uk/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/n-acetylglutamate-synthetase-deficiency/>
- National Urea Cycle Disorders Foundation  
<http://www.nucdf.org/>
- Urea Cycle Disorders Consortium  
<http://www.rarediseasesnetwork.org/cms/ucdc/Learn-More/Disorder-Definitions>

## GeneReviews

- Urea Cycle Disorders Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1217>

## ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22N-acetylglutamate+synthase+deficiency%22+OR+%22Amino+Acid+Metabolism%2C+Inborn+Errors%22>

## Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28n-acetylglutamate+synthase+deficiency%5BTIAB%5D%29+OR+%28n-acetylglutamate+synthetase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

## OMIM

- N-ACETYLGLUTAMATE SYNTHASE DEFICIENCY  
<http://omim.org/entry/237310>

## **Sources for This Summary**

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